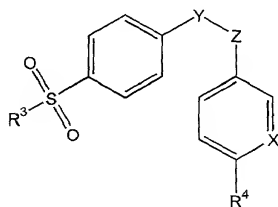


WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising one or more orally deliverable dose units, each comprising (a) a selective cyclooxygenase-2 inhibitory drug of low water solubility wherein the drug is present in solid particles having a D_{90} particle size of about 0.01 μm to about 200 μm , a sufficient portion by weight
5 of the particles being smaller than 1 μm to provide a substantially higher C_{max} and/or a substantially shorter T_{max} and/or a substantially shorter time to reach a threshold blood serum concentration for therapeutic effect, by comparison with an otherwise similar composition wherein substantially all of the particles are larger than 1 μm , and (b) a second drug selected from vasomodulators and
10 alkylxanthine compounds; wherein the selective cyclooxygenase-2 inhibitory drug and the second drug are present in total and relative amounts effective to relieve pain.
2. The composition of Claim 1 wherein the second drug is an alkylxanthine compound.
3. The composition of Claim 2 wherein the alkylxanthine compound is selected from caffeine, theophylline and theobromine.
4. The composition of Claim 2 wherein the alkylxanthine compound is caffeine.
5. The composition of Claim 1 having total bioavailability of said selective cyclooxygenase-2 inhibitory drug that is greater than that of an otherwise similar composition wherein substantially all of said selective cyclooxygenase-2 inhibitory drug particles are larger than 1 μm .
6. The composition of Claim 1 exhibiting a substantially shorter time to reach a therapeutically effective threshold blood serum concentration of said selective cyclooxygenase-2 inhibitory drug, by comparison with an otherwise similar composition wherein substantially all of the selective cyclooxygenase-2
5 inhibitory drug particles are larger than 1 μm .
7. The composition of Claim 1 wherein substantially all of said selective cyclooxygenase-2 inhibitory drug particles are smaller than 1 μm .

8. The composition of Claim 1 wherein the dose units are in the form of discrete solid articles.
9. The composition of Claim 8 wherein the solid articles are tablets or capsules.
10. The composition of Claim 1 that is in the form of a substantially homogeneous flowable mass from which single dose units are measurably removable.
11. The composition of Claim 10 wherein the substantially homogeneous flowable mass is a liquid suspension.
12. The composition of Claim 1 wherein said solid selective cyclooxygenase-2 inhibitory drug particles have a D_{25} particle size of about 450 nm to about 1000 nm.
13. The composition of Claim 1 wherein about 25% to 100% by weight of said solid selective cyclooxygenase-2 inhibitory drug particles have a particle size of about 450 nm to about 1000 nm.
14. The composition of Claim 1 wherein said solid selective cyclooxygenase-2 inhibitory drug particles have a weight average particle size of about 450 nm to about 1000 nm.
15. The composition of Claim 1 wherein the selective cyclooxygenase-2 inhibitory drug is a compound of formula

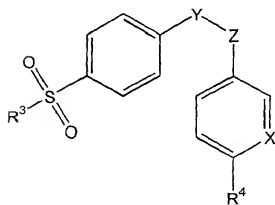


where R^3 is a methyl or amino group, R^4 is hydrogen or a C_{1-4} alkyl or alkoxy group, X is N or CR^5 where R^5 is hydrogen or halogen, and Y and Z are independently carbon or nitrogen atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups.

16. The composition of Claim 15 wherein the five- to six-membered ring is selected from the group consisting of cyclopentenone, furanone, methylpyrazole, isoxazole and pyridine rings substituted at no more than one position.
17. The composition of Claim 1 wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, 5-chloro-3-(4-methylsulfonyl)phenyl-2-(2-methyl-5-pyridinyl)pyridine, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one and (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid.
18. The composition of Claim 17 wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib.
19. The composition of Claim 18 comprising about 10 mg to about 1000 mg celecoxib in each dose unit.
20. A method of analgesia comprising orally administering, to a subject in need of analgesia, (a) a first pharmaceutical composition comprising one or more orally deliverable dose units, each comprising a selective cyclooxygenase-2 inhibitory drug of low water solubility in a therapeutically effective amount, wherein the drug is present in solid particles having a D_{90} particle size of about 0.01 μm to about 200 μm , a sufficient portion by weight of the particles being smaller than 1 μm to provide a substantially higher C_{max} and/or a substantially shorter T_{max} and/or a substantially shorter time to reach a threshold blood serum concentration for therapeutic effect, by comparison with an otherwise similar composition wherein substantially all of the particles are larger than 1 μm , and (b) a second pharmaceutical composition comprising a vasomodulator and/or an alkylxanthine compound; wherein the first and second compositions are administered in total and relative amounts effective to relieve pain.
21. The method of Claim 20 wherein the second composition comprises an alkylxanthine compound.

22. The method of Claim 21 wherein the alkylxanthine compound is selected from caffeine, theophylline and theobromine.
23. The method of Claim 21 wherein the alkylxanthine compound is caffeine.
24. The method of Claim 20 wherein the subject suffers from headache or migraine and wherein the first and second compositions are administered in total and relative amounts effective to relieve pain in the headache or migraine.
25. The method of Claim 20 wherein the first and second compositions are administered at substantially the same time.
26. The method of Claim 20 wherein the first and second compositions are administered at substantially different times.
27. A method of analgesia comprising orally administering, to a subject in need of analgesia, an effective pain-relieving amount of a composition of Claim 1.
28. The method of Claim 27 wherein the subject suffers from headache or migraine and wherein said composition is administered in an amount effective to relieve pain in the headache or migraine.
29. A pharmaceutical composition comprising one or more orally deliverable dose units, each comprising (a) a selective cyclooxygenase-2 inhibitory drug of low water solubility, wherein the drug is present in solid particles having a D_{90} particle size of about 0.01 μm to about 200 μm , and wherein about 25% to 100% by weight of the particles are smaller than 1 μm , and (b) a second drug selected from vasomodulators and alkylxanthine compounds; wherein the selective cyclooxygenase-2 inhibitory drug and the second drug are present in total and relative amounts effective to relieve pain.
30. The composition of Claim 29 wherein the second drug is an alkylxanthine compound.
31. The composition of Claim 30 wherein the alkylxanthine compound is selected from caffeine, theophylline and theobromine.
32. The composition of Claim 30 wherein the alkylxanthine compound is caffeine.

33. The composition of Claim 29 wherein substantially all of said solid selective cyclooxygenase-2 inhibitory drug particles are smaller than 1 μm .
34. The composition of Claim 29 wherein the dose units are in the form of discrete solid articles.
35. The composition of Claim 34 wherein the solid articles are tablets or capsules.
36. The composition of Claim 29 that is in the form of a substantially homogeneous flowable mass from which single dose units are measurably removable.
37. The composition of Claim 36 wherein the substantially homogeneous flowable mass is a liquid suspension.
38. The composition of Claim 29 wherein said solid selective cyclooxygenase-2 inhibitory drug particles have a D_{25} particle size of about 450 nm to about 1000 nm.
39. The composition of Claim 29 wherein about 25% to 100% by weight of said solid selective cyclooxygenase-2 inhibitory drug particles have a particle size of about 450 nm to about 1000 nm.
40. The composition of Claim 29 wherein said solid selective cyclooxygenase-2 inhibitory drug particles have a weight average particle size of about 450 nm to about 1000 nm.
41. The composition of Claim 29 wherein the selective cyclooxygenase-2 inhibitory drug is a compound of formula



where R^3 is a methyl or amino group, R^4 is hydrogen or a C_{1-4} alkyl or alkoxy group, X is N or CR^5 where R^5 is hydrogen or halogen, and Y and Z are

independently carbon or nitrogen atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups.

42. The composition of Claim 41 wherein the five- to six-membered ring is selected from the group consisting of cyclopentenone, furanone, methylpyrazole, isoxazole and pyridine rings substituted at no more than one position.
43. The composition of Claim 29 wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, 5-chloro-3-(4-methylsulfonyl)phenyl-2-(2-methyl-5-pyridinyl)pyridine, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one and (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid.
44. The composition of Claim 43 wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib.
45. The composition of Claim 44 comprising about 10 mg to about 1000 mg celecoxib in each dose unit.
46. A method of analgesia comprising orally administering, to a subject in need of analgesia, (a) a first pharmaceutical composition comprising one or more orally deliverable dose units, each comprising a selective cyclooxygenase-2 inhibitory drug of low water solubility in a therapeutically effective amount, wherein the drug is present in solid particles having a D₉₀ particle size of about 0.01 μm to about 200 μm , wherein about 25% to 100% by weight of the particles are smaller than 1 μm , and (b) a second pharmaceutical composition comprising a vasomodulator and/or an alkylxanthine compound; wherein the first and second compositions are administered in total and relative amounts effective to relieve pain.
47. The method of Claim 46 wherein the second composition comprises an alkylxanthine compound.

48. The method of Claim 47 wherein the alkylxanthine compound is selected from caffeine, theophylline and theobromine.
49. The method of Claim 47 wherein the alkylxanthine compound is caffeine.
50. The method of Claim 46 wherein the subject suffers from headache or migraine and wherein the first and second compositions are administered in total and relative amounts effective to relieve pain in the headache or migraine.
51. The method of Claim 46 wherein the first and second compositions are administered at substantially the same time.
52. The method of Claim 46 wherein the first and second compositions are administered at substantially different times.
53. A method of analgesia comprising orally administering, to a subject in need of analgesia, an effective pain-relieving amount of a composition of Claim 29.
54. The method of Claim 53 wherein the subject suffers from headache or migraine and wherein said composition is administered in an amount effective to relieve pain in the headache or migraine.
55. A pharmaceutical composition comprising one or more orally deliverable dose units, each comprising (a) a selective cyclooxygenase-2 inhibitory drug of low water solubility wherein the drug is present in solid particles having a D_{90} particle size of about 0.01 μm to about 200 μm , a sufficient portion by weight of the particles being smaller than 1 μm to provide a substantially higher C_{max} and/or a substantially shorter T_{max} and/or a substantially shorter time to reach a threshold blood serum concentration for therapeutic effect, by comparison with an otherwise similar composition in which at least 80% of the drug by weight is in the form of particles larger than 1 μm and smaller than 10 μm , and (b) a second drug selected from vasomodulators and alkylxanthine compounds; wherein the selective cyclooxygenase-2 inhibitory drug and the second drug are present in total and relative amounts effective to relieve pain.
56. A pharmaceutical composition comprising one or more orally deliverable dose units, each comprising (a) nanoparticles of a selective cyclooxygenase-2 inhibitory drug of low water solubility wherein the drug is present in

nanoparticle form in an amount to provide a substantially higher C_{\max} and/or a substantially shorter T_{\max} and/or a substantially shorter time to reach a threshold blood serum concentration for therapeutic effect, by comparison with an otherwise similar composition containing the same amount of drug as is present in the nanoparticles wherein at least 80% of the drug by weight in the otherwise similar composition is in the form of particles larger than $1\ \mu\text{m}$ and smaller than $10\ \mu\text{m}$, and (b) a second drug selected from vasomodulators and alkylxanthine compounds; wherein the selective cyclooxygenase-2 inhibitory drug and the second drug are present in total and relative amounts effective to relieve pain.

57. A method of analgesia comprising orally administering, to a subject in need of analgesia, (a) a first pharmaceutical composition comprising one or more orally deliverable dose units, each comprising a selective cyclooxygenase-2 inhibitory drug of low water solubility in a therapeutically effective amount, wherein the drug is present in solid particles having a D_{90} particle size of about $0.01\ \mu\text{m}$ to about $200\ \mu\text{m}$, a sufficient portion by weight of the particles being smaller than $1\ \mu\text{m}$ to provide a substantially higher C_{\max} and/or a substantially shorter T_{\max} and/or a substantially shorter time to reach a threshold blood serum concentration for therapeutic effect, by comparison with an otherwise similar composition in which at least 80% of the drug by weight is in the form of particles larger than $1\ \mu\text{m}$ and smaller than $10\ \mu\text{m}$, and (b) a second pharmaceutical composition comprising a vasomodulator and/or an alkylxanthine compound; wherein the first and second compositions are administered in total and relative amounts effective to relieve pain.

58. A method of analgesia comprising orally administering, to a subject in need of analgesia, (a) a first pharmaceutical composition comprising one or more orally deliverable dose units, each comprising nanoparticles of a selective cyclooxygenase-2 inhibitory drug of low water solubility wherein the drug is present in nanoparticle form in an amount to provide a substantially higher C_{\max} and/or a substantially shorter T_{\max} and/or a substantially shorter time to reach a threshold blood serum concentration for therapeutic effect, by

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comparison with an otherwise similar composition containing the same amount of drug as is present in the nanoparticles wherein at least 80% of the drug by weight in the otherwise similar composition is in the form of particles larger than 1 μm and smaller than 10 μm , and (b) a second pharmaceutical composition comprising a vasomodulator and/or an alkylxanthine compound; wherein the first and second compositions are administered in total and relative amounts effective to relieve pain.